

L5 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2005:354825 CAPLUS Full-text  
DN 143:199747

TI Polymorphous forms of rifaximin, processes for their production  
and use thereof in medicinal preparations

IN Viscomi, Giuseppe C.; Campana, Manuela; Braga, Dario; Confortini,  
Donatella; Cannata, Vincenzo; Severini, Denis; Righi, Paolo; Rosini,  
Goggreto

PA Alfa Wassermann S, Italy

SO N.Z., 27 pp.  
CODEN: NZXXBT

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	NZ 531622	A	20041029	NZ 2004-531622	20040309
	US 2005101598	A1	20050512	US 2003-728090	20031205
	CA 2460384	AA	20050507	CA 2004-2460384	20040309
	EP 1557421	A1	20050727	EP 2004-5541	20040309
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
	ZA 2004001948	A	20040429	ZA 2004-1948	20040310
	JP 2005139161	A2	20050602	JP 2004-76458	20040317
	BR 2004002382	A	20050628	BR 2004-2382	20040319
	WO 2005044823	A2	20050519	WO 2004-EP12490	20041104
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRAI IT 2003-MI2144 A 20031107

AB Disclosed herein are  $\alpha$ ,  $\beta$ , and  $\gamma$  polymorphous forms of rifaximin, wherein the formation of the  $\alpha$ ,  $\beta$ , and  $\gamma$  forms depends on the presence of water within the crystn. solvent, on the temperature at which the product is crystallized and the amount of water present into the product at the end of the drying phase. Processes for the production of  $\alpha$ ,  $\beta$ , and  $\gamma$  polymorphs of rifaximin and their pharmaceutical compns. are also disclosed. Thus, raw rifaximin 89.2 g and Et alc. 170 mL were loaded at room temperature into a three-necked flask equipped with mechanic stirrer, thermometer and reflux condenser, then the suspension was heated at  $57 \pm 3^\circ\text{C}$  until complete dissoln. of the solid. The temperature was brought to  $50^\circ\text{C}$  and then demineralized water 51.7 mL were added at this temperature during 30 min. After the end of the addition the temperature was brought to  $30^\circ\text{C}$  in one hour and the suspension was kept for 30 min at this temperature obtaining a plentiful crystallization. The temperature of the suspension was brought to  $40^\circ\text{C}$  and kept at this value during 20 h under stirring and then further lowered to  $0^\circ\text{C}$  during 30 min after which the suspension was immediately filtered. The solid was washed with 240 mL of demineralized water and dried under vacuum at  $65^\circ\text{C}$  until constant weight obtaining rifaximin  $\alpha$  46.7 g with a water content equal to 2.5 %.

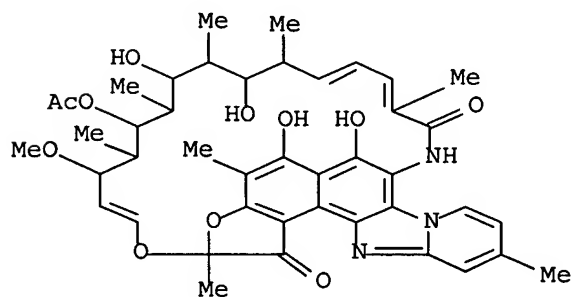
IT 80621-81-4P, Rifaximin

RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use);

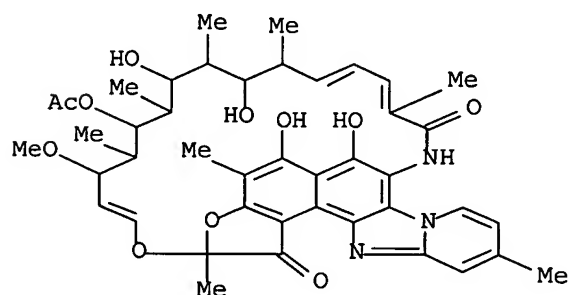
BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)  
(processes for the production of **polymorphous** forms of rifaximin  
for pharmaceutical preparation)

RN 80621-81-4 CAPLUS

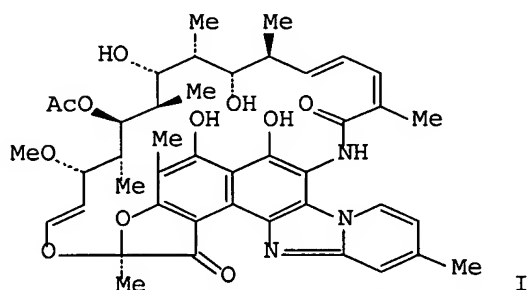
CN 2,7-(Epoxy-pentadeca[1,11,13]trienimino)benzofuro[4,5-e]pyrido[1,2-a]benzimidazole-1,15(2H)-dione, 25-(acetyloxy)-5,6,21,23-tetrahydroxy-27-methoxy-2,4,11,16,20,22,24,26-octamethyl-, (2S,16Z,18E,20S,21S,22R,23R,24R,25S,26R,27S,28E)- (9CI) (CA INDEX NAME)



L5 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1992:433790 CAPLUS Full-text  
 DN 117:33790  
 TI Application of near-infrared reflectance spectroscopy (NIRS) to several antibiotic compounds  
 AU Corti, P.; Savini, L.; Dreassi, E.; Petriconi, S.; Genga, R.; Montecchi, L.; Lonardi, S.  
 CS Dip. Farm. Chim. Tecnol., Univ. Siena, Siena, 53100, Italy  
 SO Process Control and Quality (1992), 2(2), 131-42  
 CODEN: PCQUEJ; ISSN: 0924-3089  
 DT Journal  
 LA English  
 AB The possibility of applying near-IR reflectance spectroscopy (NIRS) to the qual. and quant. control of several antibiotics was investigated. Samples of amorphous sodium ampicillin, gentamycin sulfate, erythromycin ethylsuccinate, erythromycin stearate, amorphous miokamycin and rifaximin were analyzed. Some were analyzed as primary material, others half-processed (erythromycin ethylsuccinate in granules at different concns. of active ingredient) and others as the finished pharmaceutical product (rifaximin cream). The results were both qual. and quant. satisfactory. The distinction between amorphous or crystalline sodium ampicillin and ampicillin trihydrate and between the different erythromycin ethyl succinate granules was interesting. It was confirmed that NIRS can be successfully applied to the quant. control of solid and fluid (e.g. rifaximin cream) antibiotics forms.  
 IT 80621-81-4, Rifaximin  
 RL: ANT (Analyte); ANST (Analytical study)  
 (determination of, in pharmaceuticals, by near-IR reflectance spectroscopy)  
 RN 80621-81-4 CAPLUS  
 CN 2,7-(Epoxy-pentadeca[1,11,13]trienimino)benzofuro[4,5-e]pyrido[1,2-a]benzimidazole-1,15(2H)-dione, 25-(acetyloxy)-5,6,21,23-tetrahydroxy-27-methoxy-2,4,11,16,20,22,24,26-octamethyl-, (2S,16Z,18E,20S,21S,22R,23R,24R,25S,26R,27S,28E)- (9CI) (CA INDEX NAME)



L5 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1984:503607 CAPLUS Full-text  
 DN 101:103607  
 TI Structure-activity relationships in 4-deoxypyrido(1',2'-1,2)imidazo(5,4-c)rifamycin SV derivatives  
 AU Cellai, L.; Cerrini, S.; Brufani, M.; Marchi, E.; Mascellani, G.; Montecchi, L.  
 CS Ist. Strutt. Chim. "G. Giacomello", Rome, Italy  
 SO Chemioterapia (1983), 2(5, Suppl.: Mediterr. Congr. Chemother., Proc., 3rd, 1982), 53-4  
 CODEN: CHEMEV; ISSN: 0392-906X  
 DT Journal  
 LA English  
 GI



AB The polarity of rifamycin L-105 SV (I) [80621-81-4] and its oxidized S [80621-76-7] form and the contribution of this polarity in the pharmacokinetics of these drugs were investigated. NMR and x-ray crystallog. studies indicated that the pyridoimidazo ring is coplanar with the naphthoquinonic nucleus making the pyridoimidazo ring system aromatic with the 2 N both charged. The pyrido-N is pos. charged and the other neg. charged. The contribution of charged forms to the resonance-structure of these compds. renders these agents with pharmacokinetic properties that make them virtually nonabsorbable from the intestine and thus providing high antimicrobial activity in the digestive tract.

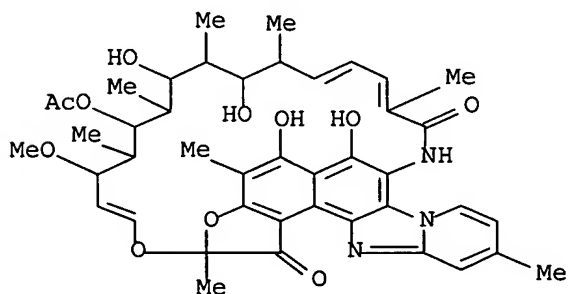
IT 80621-81-4

RL: PROC (Process)

(absorption of, by intestine, structure in relation to)

RN 80621-81-4 CAPLUS

CN 2,7-(Epoxy-pentadeca[1,11,13]trienimino)benzofuro[4,5-e]pyrido[1,2-a]benzimidazole-1,15(2H)-dione, 25-(acetyloxy)-5,6,21,23-tetrahydroxy-27-methoxy-2,4,11,16,20,22,24,26-octamethyl-, (2S,16Z,18E,20S,21S,22R,23R,24R,25S,26R,27S,28E) - (9CI) (CA INDEX NAME)



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(FILE 'HOME' ENTERED AT 19:39:26 ON 15 SEP 2005)

FILE 'REGISTRY' ENTERED AT 19:39:35 ON 15 SEP 2005

L1 1 S RIFAXIMIN/CN

FILE 'REGISTRY' ENTERED AT 19:40:29 ON 15 SEP 2005

L2 1 S 80621-81-4/RN  
SET NOTICE 1 DISPLAY  
SET NOTICE LOGIN DISPLAY

FILE 'CAPLUS' ENTERED AT 19:41:10 ON 15 SEP 2005

L3 125 S L2  
L4 125 S L1  
L5 3 S L4 AND (CRYSTAL? OR POLYMOR?)

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	19.50	29.28
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-2.19	-2.19

STN INTERNATIONAL LOGOFF AT 19:42:22 ON 15 SEP 2005